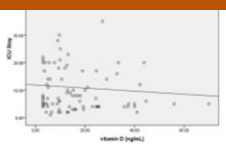

Figure 2. Showing scatter plot between Vitamin D and ICU stay (negative correlation)

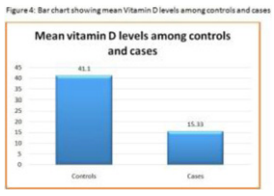

Figure 3. Bar chart showing mean Vitamin D levels among controls and cases

negative correlation. Procalcitonin levels had a positive correlation with SAPS II score, days of Mechanical Ventilation (MV), ICU LOS and mortality. The average vitamin D level in patients of sepsis in our study was 15.38 ng/dl and that of controls was 41.11 ng/dl (fig. 3) and Vit D had no significant correlation with lipid profile.

Conclusion: Deficient levels of vitamin D has a possible role in sepsis. Hence supplementation of vitamin D might have a beneficial role in sepsis management and overall outcome. Further interventional studies with larger sample size and supplementation of vitamin D is required to substantiate the findings.

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Dengue: Mathematical modelling of cytokine levels in the evoultion of severity

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Background: Dengue causes considerable morbidity and mortality in Sri Lanka. Immune mediated and cytokine related factors contribute to its evolution from an asymptotic infection to severe forms of dengue. Previous studies have analysed the association of individual cytokines with clinical disease severity. In contrast, we have viewed this evolution to severe dengue as the behaviour of a complex dynamic system. We therefore analysed the combined effect of multiple cytokines that interact dynamically with each other in order to generate a mathematical model to predict the occurrence of severe dengue. We expect this to have predictive value in detecting severe cases and improve outcomes.

Methods & Materials: We analysed data on 11 adult patients with dengue fever (DF) and 25 patients with dengue haemorrhagic fever (DHF) recruited from the Colombo South Teaching Hospital, Sri Lanka. Platelet activating factor (PAF), sphingosine 1- phosdetect factors that correlated with each other. Their interactions were mapped using Fuzzy Logic mechanisms with the combination of Hamacher and OWA operators.

Results: Clustering indicated that S1P and IL1β levels were associated with each other. Since, PAF, IL-10 and TNF-α have shown to associate with severe dengue, they were combined together by allocating these cytokines a higher prominence in the model. Operator value below 0.3 in the overall model correctly predicted development of DHF with 76.6% accuracy. A region of ambiguity was detected in the model for the value range 0.35 to 0.55. However, in six instances patients with DHF indicated operator values above 0.6 and in four instances, patients with DF showed operator values below 0.35. The accuracy of this model in predicting severe dengue was 76.19% at 96 hours from the onset of illness, 75% at 108 hours and 74.07% at 120 hours.

Conclusion: The results show a robust mathematical model that explains the evolution of dengue infection to its serious forms. This model should be further improved by including additional parameters and be validated on other data sets.

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Engineering of measles virus to target cancer cells, an attempt

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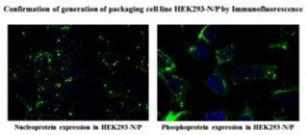
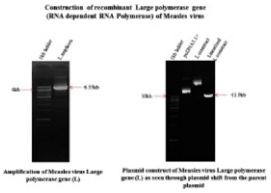
Background: Regardless of general perception as potentially dangerous pathogens, viruses have been exploited and used as vaccine agents or as carriers for gene therapy. Similar positive effects have been observed in case of cancer patients getting infected with viruses, where infection has resulted in temporary tumor regression. Hence, the development of a recombinant virus that selectively infects and kills cancer cells can be a promising anticancer tool in near future. Here we made an attempt to generate an oncolytic virus using Measles viral genome (Edmonston strain) backbone and to further arm this recombinant virus with non viral genes of known anti-proliferative activity to enhance its antitumor activity.

Methods & Materials: Genes encoding Nucleoprotein (N) and Phosphoprotein (P) of Measles virus were cloned into expression vector pcDNA(3.1+). HEK293 cells were stably transfected with viral N and P constructs to generate a packaging cell line for the recovery of recombinant virus. Gene encoding viral L polymerase (RNA-dependent RNA polymerase) was cloned in pcDNA(3.1) and co-transfected with the Measles viral full-length genome construct (Addgene #58748) in packaging cell line to enable the generation of viral negative sense genome. For arming of the virus, the gene encoding a pro-apoptotic protein BNiP3 of human origin will be inserted into the recombinant Measles viral genome upstream of Matrix gene.

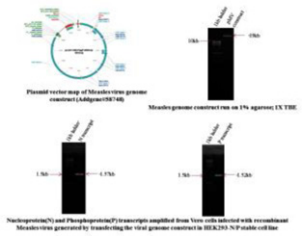
Results: Co-expression of measles virus N and P proteins in packaging cell line (HEK293-N/P) was confirmed by IFA staining (Fig1). Gene encoding L polymerase construct was generated (Fig 2). Expression of viral genes in packaging cells transfected with full-length viral genome was confirmed at transcript and protein levels. Further, expression of viral genes in Vero cells infected with the lysates recovered from packaging cells transfected with the recombinant viral genome confirmed its replication competency (Fig 3).



Expression of Nucleoprotein and Phosphoprotein of Measles virus in the packaging cell line



Generation of L polymerase plasmid construct of Measles virus



Infection of Vero cells with recombinant Measles virus generated in the packaging cell line

Conclusion: The components required for the construction of an oncolytic Measles virus were successfully generated. Studies are ongoing to rescue the recombinant virus from packaging cell line and to further arm the recombinant Measles virus with BNiP3and validate its anti-tumor activity. This study is aimed towards finding the therapeutic potential for an infective virus particle reprogrammed to emerge as an alternative to conventional anti-cancer therapy.

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Prevalence of otitis media and its hearing loss in children of South Indian population

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Background: Otitis media (OM) refers to bacterial infection or an inflammation of middle ear cleft in younger children than adults. The effusion of fluids in the middle ear or pathological changes in the tympanic membrane or ossicles leads to hearing loss. The aetiopathogenesis of OM is due to the involvement of multiple factors such as demographic, genetic, environmental and other health related factors like infections, allergy, asthma, eustachian tube dysfunction, cleft palate, and adenoid hypertrophy etc., Therefore, the present study aimed to determine the prevalence of OM subtypes and its association with hearing loss in children of South Indian population.

Methods & Materials: All the 896 patients with otitis media seen in MAA ENT Hospitals, Hyderabad, Telangana State, from 2010 - 2014 constituted the study subjects. The patients whose age ranged from 1-15 years with symptoms such as otalgia, otorrohea/ inattentiveness and clinical examination which showed fluid behind intact tympanic membrane supported by 'B' type/high gradient tympanometry constituted the study subjects. The chi-square test was used for comparing the proportions of categorical variables by using Statistical Package for Social Sciences, PASW STATISTICS 18.0 software (SPSS Inc., Chicago, IL, USA).

Results: Out of 896 OM patients, Acute supparative otitis media(ASOM) were 15.5%, chronic supparative otitis media(CSOM) were 65.3% and otitis media with effusion(OME) were 19.2% with male preponderance of 1.8:1. With regard to seasonal variability, the occurrence of OM was more during winter. The occurrence of ASOM and CSOM was more unilateral except in OME which showed bilaterality. It was also observed that more prevalence of sensorineural form is noticed in ASOM and OME while mixed form in CSOM.

Conclusion: CSOM is one of the most common inflammatory disorders of middle ear and has an important health concern in children. Continuous efforts in the treatment of hearing impairment rehabilitation are to be taken for the proper management of OM. Therefore, OM is a condition of serious pediatric concern, research on the genetic aspects may help to understand the underlying mechanisms for formulating better therapeutic and preventive strategies.

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